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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/627,631	07/28/2003	Marc Achen	28967/56801D	3314

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EXAMINER	
HUYNH, PHUONG N	

ART UNIT	PAPER NUMBER
1644	

MAIL DATE	DELIVERY MODE
03/28/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/627,631	ACHEN ET AL.	
	Examiner	Art Unit	
	PHUONG HUYNH	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *three* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *28 February 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *9-13,41 and 45-47* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *9-13, 41 and 45-47* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. Claims 9-13, 41 and 45-47 are pending and are being acted upon in this Office Action.

2. Applicant's request filed 2/28/08 for reconsideration of the finality of the rejection of the last Office action is persuasive and, therefore, the finality of that action is withdrawn.

3. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter, which the applicant regards as his invention.

4. Claims 9-13, 41 and 45-47 stand rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps. See MPEP § 2172.01. The omitted step in claim 45 between (a) and (b): exposing said sample with an antibody that specifically binds to the unprocessed full-length VEGF-D of SEQ ID NO: 2, see page 27 paragraph [0059]. The remaining claims are rejected for depending from said rejected claim 45.

Applicants' arguments filed 2/28/08 have been fully considered but are not found persuasive.

Applicants' position is that one of skill in the art would appreciate upon review of the specification how to measure the amount and size of VEGF-D in the sample as recited in claim 45. Moreover, contacting the sample with an antibody that binds unprocessed VEGF-D is one variation described in the specification, but it is not the only way for a person of ordinary skill to measure the amount and size of VEGF-D. (For example, the VEGF-D could be purified and then measured using conventional protein sizing and quantification techniques, or a different affinity reagent, such as a VEGF-D receptor peptide, could be used).

In response, the specification discloses only the use of antibody that binds to unprocessed VEGF-D for a method of diagnosing growth characteristics of a neoplastic disease in an organism by detecting unprocessed VEGF-D using antibody that binds to unprocessed VEGF-D of SEQ ID NO: 2. The specification does not disclose purified VEGF-D from the sample and then measured using conventional protein sizing and quantification techniques, or a different affinity reagent, such as a VEGF-D receptor peptide for the claimed method as argued. See *Liebel-Flarsheim Co. v. Medrad Inc.*, 358 F.3d 898, 906, 69 USPQ2d 1801, 1807 (Fed. Cir. 2004)(discussing recent

cases wherein the court expressly rejected the contention that if a patent describes only a single embodiment, the claims of the patent must be construed as being limited to that embodiment);< *E-Pass Techs., Inc. v. 3Com Corp.*, 343 F.3d 1364, 1369, 67 USPQ2d 1947, 1950 (Fed. Cir. 2003)

5. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office Action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

6. Claims 9-13, 41 and 45-47 stand rejected under 35 U.S.C. 102(b) as being anticipated by WO 99/33485 publication (of record, published July 8, 1999, PTO 1449).

The WO 99/33485 publication teaches a method for diagnosing neoplastic disease such as human malignant melanoma as an indicator of future metastatic risk. The reference method steps comprise: obtaining a sample such as a biopsy tissue specimen from human patient with melanoma (See page 20, lines 1-10, page 32 at line 18, in particular), exposing the biopsy specimen to a composition comprising an antibody such as monoclonal antibody 4A5 (later renamed as VD1 as evidenced in page 48 of instant specification that bind specifically to unprocessed (full-length) VEGF-D) for immunohistochemistry analysis (See page 32, lines 18-19, in particular), measuring the presence or increase (amount) in the VEGF-D expression in or around a potential neoplastic growth (See pages page 20, lines 1-10, pages 33-35, Figs 7A-E, claims 28-30, in particular). The reference teaches VEGF-D monoclonal antibodies detected VEGF-D in melanoma cells in both clinical samples, and the detection of VEGF-D indicates these tumor cells are most likely producing said VEGF-D (See page 35, lines 13-15, in particular). The recitation of measuring the size of the VEGF-D polypeptide is inherently to the reference antibody since the reference antibody 4A5 binds to the unprocessed VEGF-D or full-length (VEGF-D) in the sample. Further, as evidenced at pages 48-49 of instant application, the antibody used by applicant to detect the "size" of VEGF-D in formalin fixed and paraffin embedded tissue section (immunohistochemistry) is the same antibody used for immunohistochemistry as that of the WO 99/33485 publication. The reference antibody includes a detectable label such as Streptavidin-alkaline phosphatase, enzyme labels such as horseradish peroxidase, or fluorimetric labels such as fluorescein-5-isothiocyanate (FITC) (see pages 20, 33,

claim 30 of the WO 99/33485, in particular). The increase amount of VEGF-D is evidenced by the more pronounced staining in small islands of tumor cells at the periphery of the invasive portion of the tumor, which correlates with increased tumor growth or metastatic risk (see page 34, lines 8-15, Figure 7A-B, in particular). Claim 47 is included in this rejection because the reference teaches VEGF-D is stained positively in the cytoplasm of the endothelial cells in the tumor section (see page 34, line 18-20, Figure 7C, page 35, line 15-21, in particular). Claim 41 is included in this rejection because the WO 99/33485 publication teaches breast cancer associated with lymph node metastasis and obstruction; increasing amount of the VEGF-D induces lymphangiogenesis (see page 17, line 11-17, in particular).

Applicants' arguments filed 2/28/08 have been fully considered but are not found persuasive.

Applicants' position is that Achen II (WO 99/33485) teaches that 4A5 antibody was generated against a processed form of VEGF-D known as VEGF-DΔNΔC. Because antibody 4A5 binds to the processed VEGF-D, the in situ experiments cited by the Examiner cannot be fairly interpreted as a measurement of the quantity of unprocessed VEGF-D.

In response, although the reference 4A5 was made against a processed form of VEGF-D, the reference antibody 4A5 also cross-reacts with full-length unprocessed and processed form of VEGF-D. This is evidenced in the specification at pages 44-45 of instant specification, paragraphs 0114-0115 and example 2.

7. New ground of rejection is set forth below.

8. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

9. Claims 9-13, 41 and 45-47 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor, at the time the application was filed, had possession of the claimed invention. **This is new matter**.

The recitation of "*size* of the VEGF-D" in claim 45 has no support in the claims and specification as filed. The specification discloses "unprocessed full-length VEGF-D polypeptide having the sequence of SEQ ID NO: 2", see page 28, paragraph [0065]. The specification discloses only human VEGF-D of SEQ ID NO: 2. The unprocessed human VEGF-D is about 53 kd, see page 45, paragraph 0113.

The specification does not disclose the size of any VEGF-D for the claimed method.

10. No claim is allowed.

11. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Phuong Huynh, Ph.D. whose telephone number is (571) 272-0846. The examiner can normally be reached Monday through Thursday from 9:00 a.m. to 6:30 p.m. and alternate Friday from 9: 00 a.m. to 5:30 p.m. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Eileen B O'Hara can be reached on (571) 272-0878. The IFW official Fax number is (571) 273-8300.

12. Any information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/Phuong Huynh/
Primary Examiner, Art Unit 1644
March 24, 2008

Application Number	Application/Control No.	Applicant(s)/Patent under Reexamination	
	10/627,631	ACHEN ET AL.	
	Examiner	Art Unit	
	PHUONG HUYNH	1644	